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RMS Patent Department

NO. 051 P. 6

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Serial No. 10/635,171
Response to Non-Final Action
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Amendments to the Drawings:

The attached twelve (12) sheets of drawings includes changes to Figs. 1-7. The drawings have been amended to more clearly show the headings and numbers on the x- and y-axes. No new matter is added by these amendments, and the amendments comply with the requirements of §§1.84 and 1.121(d). Accordingly, entry of the Replacement Sheets is respectfully requested.

Attachment: Replacement sheets (12)

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Remarks:

Claims 1-27 are pending in the present application. By this Amendment, claims 2, 3, 11-13, and 16-26 are canceled. Claims 1 and 27 are amended. Support for the amendments to the claims are found in the specification as originally filed, as the amendment to claim 1 incorporates all the limitations of originally filed claim 3, and the amendment to claim 27 incorporates language derived from claim 1, from which it depends. No new matter is added to the claims by these amendments. Accordingly, entry of the amendments to the claims is respectfully requested.

Objections to the drawings:

The drawings were objected to on the grounds that the headings and the numbers on the x- and y-axes were unclear. Applicants herewith present Replacements Sheets for Figures 1-7 in which the requested changes have been made. These sheets replace the original sheets for Figures 1-7. Entry of the Replacement Sheets for Figures 1-7 is respectfully requested.

Claim objections:

Claims 15 and 27 were objected to for referring to "the pair of hybridization probes of claim 1", while that claim refers instead to a "composition comprising a pair of FRET hybridization probes". Claims 15 and 27 are amended to correct the language to refer to the composition comprising the probes rather than to the probes themselves. As noted above, this language is derived from that of claim 1, and so no new matter is added by this amendment. Therefore, withdrawal of the objection to claims 15 and 27 is respectfully requested.

Claim Rejections under 35 U.S.C. 112:

Claims 1 and 13 were rejected under 35 U.S.C. 112, first paragraph, on the ground that the specification did not provide enablement for two spacer probes that interact in an ionic manner. While not admitting to the propriety of the rejection, and solely to expedite prosecution of the application, Applicants have chosen to amend claim 1 to specifically recite that the noncovalent interactions are A/T base pair interactions. Support for such a limitation is found throughout the specification, particularly in Examples 2-8. Claim 13

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has been canceled, rendering the rejection of that claim moot. Accordingly, withdrawal of the rejection of claim 1 under 35 U.S.C. 112 is respectfully requested.

Claim Rejections under 35 U.S.C. 102:

Claims 1-3, 5, 10, and 27 were rejected under 35 U.S.C. 102(b) as anticipated by US Patent 6,130,047 (Nadeau et al.). While not admitting to the propriety of the rejection, and solely to expedite prosecution of the application, Applicants have chosen to amend claim 1 to recite that the spacer entities of the FRET hybridization probes are capable of forming non-covalent interactions with each other, wherein these non-covalent interactions consist essentially of A/T base pair interactions. The Action states that Nadeau et al. teach spacer entities that consist of 2 A/T base pairs in combination with 5 G/C base pairs (reference, Example 3). However, such sequences are prone to the problem discussed in the present application; namely, the quenching or dequenching effects of G residues on FRET pair signal intensities (see present application, page 2, line 20 to page 3, line 3). The presence of the 5 G/C base pairs in the spacer entity in Nadeau et al. illustrates this problem. Looking at the Table in column 18, one can see that compared to the single dye pair arrangement, the 3-way junction exhibits a much higher pre-extension fluorescence intensity (3200 vs. 1300). The ratio of pre-extension fluorescence intensities (2.5; equal to 3200/1300) is much higher than the ratio of post-extension intensities (1.7; equal to 6800/4000), suggesting a dequenching effect of the G residues present in the spacer entity. The ratio of post-extension fluorescent intensity to pre-extension intensity of the 3-way junction (2.1; equal to 6800/3200) is much lower than that of the single dye pair arrangement (3.1; equal to 4000/1300). Therefore, although the absolute signal change is higher than in the case of the 3-way junction than in the case of the single dye pair arrangement, the signal/noise ratio (defined as the ratio of post-extension fluorescent intensity to pre-extension intensity) is lower for the 3-way junction.

In contrast, the presently claimed invention eliminates the unpredictable effects of G residues, by requiring that the spacer entity consist only of A/T base pairs. This element is neither taught nor suggested by Nadeau et al. Accordingly, reconsideration and withdrawal of the rejections of claims 1-3, 5, 10, and 27 under 35 U.S.C. 102(b) are respectfully requested.

Claim Rejections under 35 U.S.C. 103(a):

Claim 4 was rejected under 35 U.S.C. 103(a) as obvious over Nadeau et al. in view of Wittwer et al. (US Patent No. 6,140,054). Claims 6 and 7 were rejected as obvious over

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Nadeau et al. in view of Fisher (US Patent No. 6,054,568). Claims 8 and 9 were rejected as obvious over Nadeau et al. in view of Acton et al. (US Patent No. 6,228,581). Claims 11 and 12 were rejected as obvious over Nadeau et al. in view of Ogawa et al. (J. Amer. Chem. Soc.). Claim 14 was rejected as obvious over Nadeau et al. in view of Urdea et al. (US Patent No. 5,635,352). Claim 15 was rejected as obvious over Nadeau et al. in view of Ahern (The Scientist). The rejections are respectfully traversed.

Claims 11 and 12 are by this Amendment canceled, rendering their rejections moot. With regard to the other rejections, as noted above, Nadeau et al. neither teaches nor suggests an element of the claims as amended. Furthermore, none of the other references cited in the Action teach or suggest anything relating to the quenching or dequenching effects of G residues on FRET pair signal intensities. Accordingly, reconsideration and withdrawal of the rejections of claims 4, 6-9, 14 and 15 under 35 U.S.C. 103(a) are respectfully requested.

Conclusion:

In view of the above, Applicants believe all claims now pending in this Application are in condition for allowance. Applicants hereby request a two-month extension of time for responding to the Office Action. The Commissioner is hereby authorized to charge the extension of time fee (large entity) of \$450.00 under 37 CFR 1.17 to Account No. 50-0812. The Commissioner is further authorized to charge any fee deficiency, or credit any overpayment, to Deposit Account No. 50-0812.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned directly at 510-814-2891.

Respectfully submitted,

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